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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/542,718	04/04/00	YU H	6687.US.01

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EXAMINER	
JOHANNSEN, D	
ART UNIT	**PAPER NUMBER**
1655	6

DATE MAILED: 10/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/542,718	Yu et al
Examiner	**Group Art Unit**
Diana Johannsen	1655

☒ Responsive to communication(s) filed on *Aug 8, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Claim Objections

1. Claims 4 is objected to because of the following informalities. In claim 4 (b), the phrase "conditions to generate at an amplification product" should be amended to recite "conditions to generate an amplification product".Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite for failing to recite a final process step that clearly relates back to the claim preamble, and over the recitation of the term "a target sequence" and "the target sequence". The claim is drawn to a "method of amplifying a β2 adrenergic receptor target sequence", yet recites a final process step of subjecting a mixture to amplification conditions "to generate at least one copy of the target sequence". However, as step (a) of the claim refers to "a test sample suspected of containing a target sequence" (rather than, e.g., "a test sample suspected of

containing said target", or "a test sample suspected of containing a β2 adrenergic receptor target sequence"), it is unclear as to whether the claim is intended to be directed to a method for amplifying a β2 adrenergic receptor target sequence, or to a method for amplifying any "target sequence". Clarification is required.

Claim 6 is indefinite over the recitation of "SEQ ID NO 6" and "SEQ ID NO 7". As no such sequences are described or disclosed elsewhere in the specification or Sequence Listing, it is unclear as to what sequences might be encompassed by this reference. Clarification is required.

Claim Rejections - 35 U.S.C. § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Drazen et al (WO98/39477 [9/1998]).

Drazen et al teach the human β2-adrenergic receptor gene (see, e.g., p. 4, SEQ ID NO: 2). It is an inherent property of this gene that it is a "composition of matter comprising SEQ ID NO: 2 and SEQ ID NO: 3" as required by claim 1. Furthermore, Drazen et al disclose that the wild-type gene further comprises instant SEQ ID NO: 4, and that a variant gene comprising a

codon 16 polymorphism comprises instant SEQ ID NO: 5 (see p. 4, SEQ ID NO: 2). Accordingly, Drazen et al clearly anticipate the instant claims.

Claim Rejections - 35 U.S.C. § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dewar et al (J. Allergy Clin. Immunol. 100(2):261-265 [8/1997]) in view of Drazen et al (WO98/39477 [9/1998]) and Matalon et al (U.S. Patent No. 5,679,635 [10/1997]).

This rejection applies to claims 1-2 as they may be limited to a composition of matter comprising a primer pair consisting of SEQ ID NO: 1 and SEQ ID NO: 2 (claim 1) and further comprising a probe selected from SEQ ID NO: 4 and SEQ ID NO: 5 (claim 2). Dewar et al teach a method for specific detection of codon 16 and codon 27 polymorphisms in the human β2 adrenergic receptor gene (see entire reference). In Dewar et al's method, a primer pair is used to specifically amplify a region of the gene encompassing both polymorphisms, and the polymorphisms are detected by hybridization of amplification products with allele specific probes (p. 262-263). Dewar et al do not teach or suggested selecting primers consisting of or comprising SEQ ID NOs 2 or 3, or allele specific probes consisting of SEQ ID NOs 4 or 5, for use in their

methods. Drazen et al teach the sequence of the human β2-adrenergic receptor gene, and further teach a variant gene comprising the codon 16 polymorphism discussed by Dewar et al (see, e.g., p. 4, SEQ ID NO: 2). An examination of the β2 adrenergic receptor gene taught by Drazen et al reveals that instant SEQ ID NO: 2 targets a site approximately 50 nucleotides downstream from the forward primer taught by Dewar et al, that instant SEQ ID NO: 3 targets a site approximately 80 nucleotides upstream from the reverse primer taught by Dewar et al, and that instant SEQ ID NOs 4 and 5 overlap, but are not identical to, the allele specific probes taught by Dewar et al. Drazen et al disclose that detection of the codon 16 polymorphism alone may be used to assess risk "for adverse reaction to chronic β-agonist administration" (see entire reference, especially, e.g., p. 2). Accordingly, Drazen et al provide additional motivation to one of ordinary skill in the art to detect the codon 16 mutation in the β2 adrenergic receptor gene. While the method of Dewar et al accomplishes detection of the codon 16 mutation, detection of the codon 16 mutation alone (as opposed to both the codon 16 and codon 27 mutations) would require amplification of a shorter segment of the β2 gene, and would therefore require less time (i.e., shorter amplification cycles) and fewer reagents than the method of Dewar et al. Thus, in view of the teachings of Drazen et al, an ordinary artisan would have been motivated to have modified the method of Dewar et al so as to have detected codon 16 alone for the advantage of rapidly identifying individuals who may be at risk for reacting to β-agonist administration while simultaneously saving time and reagents as compared to the method of Dewar et al. With respect to selection of appropriate primers and probes for use in such a method, Matalon et al teach that design,

selection and production of suitable probes and primers for use in PCR and allele specific hybridization is routine in the art (col 14, lines 26-38). For example, Matalon et al state that "suitable probes for detecting a given mutation include the nucleotide sequence at the mutation site and encompass a sufficient number of nucleotides to provide a means of differentiating a normal from a mutant allele", and that "suitable PCR primers are complementary to sequences flanking the mutation site" (col 14, lines 26-38). Accordingly, the combined teachings of Dewar et al, Drazen et al, and Matalon et al suggest a variety of primers and probes consisting of sequences taught in the art, including those claimed by Applicant, that could have been used successfully in methods of detecting codon 16 polymorphisms in the β2 adrenergic receptor gene by amplification and allele specific hybridization. Absent a showing of unexpected results with the particular primers and probes of the instant claims, the use of any primers flanking codon 16 and any allele specific probes targeting codon 16 in the β2 adrenergic receptor gene would be obvious over Dewar et al in view of Drazen et al and Matalon et al. With further respect to claims 5-6, it is noted that Drazen et al teach kits comprising a variety of reagents for detection of the codon 16 polymorphism in the human β2 adrenergic receptor gene, including primers and other amplification reagents (p. 7-8, 28-29). An ordinary artisan would have been motivated to have packaged reagents for use in the method suggested by Dewar et al in view of Drazen et al and Matalon et al into kits for the advantage of providing practitioners with all the reagents necessary to carry out the method in a convenient and cost-effect format.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

September 25, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600